SPECIFIC FEATURES OF THE EFFECT OF THE HEPARIN DRUG

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Abstract. *Heparin is a life-saving drug, which belongs to few clinically used drugs without defined molecular structures in modern medicine. Heparin is the mostly negatively charged biopolymer with a broad distributions in molecular weight, charge density, and biological activities. Heparin is mainly composed of repeating trisulfated disaccharide units, which is made by mast cells that are enriched in the intestines, lungs or livers of animals. Porcine intestines and bovine lungs are two mostly used sources for heparin isolation. Heparin is well known for its anticoagulant and antithrombotic pharmacological effects. The anticoagulant activity of heparin is attributable to a 3-O-sulfate and 6-O-sulfate containing pentasaccharide sequence or a minimum eight-repeating disaccharide units containing the pentasaccharide sequence that catalyzes the suicidal inactivation of factor Xa or thrombin by a serpin or serine protease inhibitor named antithrombin III, respectively.*

Keywords: *thrombocytopenia, anticoagulant, antithrombin, encephalopathy*

Heparin is a highly-sulfated glycosaminoglycan (GAG), which was discovered by Jay McLean and William Henry Howell in 1916. It is one of the oldest drugs used as the anticoagulant and antithrombotic medicines for more than 80 years since it passed the clinical trials in 1935.1, 2, 3 Heparin is still an essential drug for modern medicine. The anticoagulant properties of the glycosaminoglycan heparin have made it an invaluable drug for the prophylaxis and treatment of thrombosis. These properties result from the ability of the polysaccharide to enhance the rate of inactivation of blood coagulation proteinases by their natural protein inhibitors, the most important of which is antithrombin. Recognition of the complex multifaceted beneficial effects of heparin underscores its therapeutic potential in various clinical situations. In this review we focus on the anticoagulant and nonanticoagulant activities of heparin and, where possible, discuss the underlying molecular mechanisms that explain the diversity of heparin's biological actions. An understanding of the molecular mechanisms underlying the antithrombotic action has allowed the dissociation of the specific anticoagulant effects of heparin from other nonspecific interactions with plasma proteins, platelets and the vascular endothelium, which contribute to certain undesirable features of heparin anticoagulant therapy. However, in 2007–2008, contaminated heparin was associated with hundreds of anaphylactic reactions and more than 100 fatalities in the United States.5, 6, 7, 8, 9 There is a rising concern about the

safety and supply security of heparin. At beginning, heparin was isolated from canine or bovine livers for commercial production. Subsequently, porcine mucosa and bovine lungs were mainly used for heparin production.10, 11 Due to the outbreak of bovine spongiform encephalopathy (BSE) in the UK in 1996 plus less heparin-induced thrombocytopenia and thrombosis (HITT) side-effects associated with heparin from porcine intestinal mucosa, bovine heparin production has been significantly reduced.

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